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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,793	09/19/2003	Edward J. Kaplan	KAP 100 CIP	6738

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	
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09/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,793	KAPLAN, EDWARD J.	
	Examiner	Art Unit	
	JAGADISHWAR R. SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/02/2008; 12/29/2003; 07/13/2004 & 08/02/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of amendment filed on 05/16/2008. Upon entering the amendment, the claim 44 is amended and claims 36-55 are currently pending and presented for examination.

Information Disclosure Statement

2. The Information Disclosure Statement filed on 04/02/2008 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office Action.

Response to Arguments

3. Applicant's arguments filed on 05/16/2008 with respect to claims under U.S.C. 35 103(a) rejection have been fully considered but they are not persuasive. The 103(a) rejection of Zamora et al (US 2001/0044567 A1) and Grimm (US 6,010,446) in view of Coniglione (US 5,713,828) is maintained and made **FINAL**.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 36-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zamora et al. (US 2001/0044567 A1) and Grimm (US 6,010,446) in view of Coniglione (US 5,713,828).

4. Zamora discloses a brachytherapy device comprising a biocompatible biodegradable component (i.e. polymeric material), a non-radioactively therapeutic component and a biodegradable radiopaque marker (see abstract). The biodegradable component includes polymers (e.g. Poly (D,L-lactide) poly (L-lactide, (polyglycolide, poly (L-lactide-co-glycolide) that are same as those claimed (see page 2, para 0025 and page 5, para 0055). And also the biocompatible polymer such as poly (hydroxybutyrate) is included that can read as biocompatible elastic Carrier to form an elastic brachytheraphy seed (see page 4, para 0049) since they are essential same compounds. The size and shape of the seeds are within the scope of those claimed (see page 5, para 0057+). And also the outer surface of device have sufficient permanence or persistence so that the radioactive source material remains localized at the site of implantation at all times for use in treatment of diseases, including radiation therapy of cancers (see 0029 and 0031). The non-radioactive therapeutic component

includes chemotherapeutic agent such as cisplatin bleomycin, a radiosensitizer drug such as 5-halo uracil compounds (see page 7, para 0080). Zamora also teaches the radiopaque marker which includes various markers that are biodegradable such as platinum, tantalum and bismuth (see page 4, para 0051), where these markers are same as one required by claims, thus non-radionuclide imaging marker requirement is inherently met. The seeds of the device may be implanted singly, or may utilize suture strands, webs, meshes or other means to group the devices in a desired manner (see page 7, para 0085+). Methods of making the seeds are disclosed on pages 5-8, which include the steps as claimed.

Grimm discloses a spacer element for use between radioactive seeds in needle implant treatment for prostate cancer, comprising: a spacer element having a center section and two end sections, the two end sections being configured, respectively, to hold an adjacent radioactive seed such that a spaced plurality of radioactive seeds results from the connection of successive spacers and seeds; wherein the spacer element is made from a material which is absorbable in living tissue; and wherein a combination of spacer element and radioactive seeds can be fitted within a needle for subsequent insertion into the prostate treatment thereof (see col. 1 lines 65+).

Zamora and Grimmer fails to disclose one or more biodegradable structures effective to prevent migration and one more compliant setal structures which impart adhesive properties upon implantation of the seed into a target tissue.

Coniglione discloses a radioactive seed for interstitial implantation brachytherapy device formed from a hollow-tube-shaped seed-substrate, allowing the easy association

of the device with suture material. And also discloses that shaped device minimizes the chance of migration of implanted seeds due to better attachment to tissue (see abstract). And also the entire device is provided with a biologically compatible, radiation-permeable, surface-sealing layer having perforations through the walls of the tube, and the perforations may be oriented in any direction. And also discloses the hallow-tube design of the device permits the growth of tissue into the device to anchor the device at the application site and minimize the potential for migration (see col5. lines 48-54). And further discloses the brachytherapy device has special application to the form of brachytherapy wherein seeds are associated with flexible suture material and are thereby held in a compliant array in the neoplastic tissue by the suture while their radiation dose is delivered (see col.5 lines 1-5).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate brachytherapy seeds having one or more biodegradable structures effective to prevent migration and one more compliant setal structure which impart adhesive properties upon implantation of the seed into a target tissue disclosed by Zamora and Grimmer. In view of Coniglione, motivation would come from the brachytherapy device disclosed specifically intended to ease the task of surgeons, urologists, radiation therapists, radiologists, and others who use brachytherapy, e.g. the interstitial implantation of radioactive sources into tumorous tissue for the purpose of irradiating and thus killing malignant cells.

When these references are taken together, one would have been motivated to extend Coniglione's teaching to add brachytherapy seeds having one or more

biodegradable structures effective to prevent migration and one more compliant setal structure which impart adhesive properties upon implantation of the seed into a target tissue to maximize therapeutic efficacy. As suggested by cited references, one would have reasonably expected successful addition of Coniglione's brachytherapy seeds such as a hollow-tube shaped substrate that have perforations through the walls of the tube) because the effectiveness, extra benefits (i.e., minimize the potential migration of seeds, and flexibility of the device allows a surgeon to effectively react to challenges not revealed by the presurgical workup of the patient) and safety are already well proven and are well suggested by latter reference cited.

One would have been motivated to do so, with reasonable expectation of success because it is always desirable to have extended therapeutic modalities to improve patient's compliance by enhancing patient satisfaction and increasing the selection option. The techniques and skills required for making such substitution is conventional knowledge or well within the skills of ordinary artisan as evidenced by these references cited.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities, and pertinent to the problem which applicant concerns about. MPEP 2141.01 (a).

Applicant's arguments filed on 05/16/2008 have been fully considered but they are not persuasive.

Applicant asserts that Zamora or Grimm in view of Coniglione does not disclose any structure attached to the seed to maintain its location upon implantation.

This argument is not persuasive since the recitation; one or more means to maintain location or orientation of the seed upon implantation in claim 36 is very broad. Further, suitable brachytherapy seeds for implantation into the tumorous tissues are well known in the art. Fabrication methods and techniques permit the construction of brachytherapy seeds having a variety of forms or shape or otherwise minimize the chance of migration of implanted seeds within a patient's body away from the initial site of implantation or insertion. Zamora discloses method and improved delivery devices to deliver local radiation, and chemotherapeutic or bioactive drugs, and after implantation so that the radioactive source material localized at the site of implantation at all times while emitted radiation remains significant (see para 0029). And also the brachytherapy devices disclosed by Zamora are made such that the density of the device approximates that of normal and cancerous tissues or frequently have a greater density than that of the tissue within which they are placed. By approximating the density of the tissue in which the devices are placed, movement of the devices within the body is minimized (see para 0083). And also the device disclosed by Zamora would retain integrity throughout the period of active emission of radiation.

Applicant also asserts that Zamora does not disclose a degradable radiopaque marker.

This argument is not persuasive since, Zamora does disclose radiopaque material capable of being detected by X-rays and conventional radiographic methods.

Preferred iodine-containing radiopaque agents include iodixanol, iohexol, iodophthalein sodium, and metal containing contrast agents such as barium sulfate and bismuth trioxide, which can be mixed with polymers such as polyurethane to increase radiocapacity and the like (see para 0051).

Applicant also asserts that Zamora or Coniglione does not disclose or suggest for means of maintain the seed at the desired location.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combination of references. See in re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981): In re Merck & Co., 800 F.2d 1091, 231 USPA 375 (Fed.Cir.1986).

In this case, the Coniglione patent is relied upon to show that it is known in the art to manufacture radioactive seeds for interstitial radiotherapy of malignant neoplasms or other diseases treatable with radiation. Coniglione discloses a brachytherapy device is a hallow-tube shaped seed substrate capable of attaching to the tissue and minimizes the chance of migration of implanted seeds within a patient's body. And in one embodiment, the walls of the hallow-tube seed substrate have perforations oriented randomly and would assist as anchor points as tissue grows into the holes and prevent in migration of seeds from the implantation in the patient's body. And further Coniglione provide an improved treatment of medical conditions such as neoplastic diseases according to the normal practice of brachytherapy, e.g., the interstitial implantation of radioactive sources into tumorous tissue for the purpose of irradiating and thus killing malignant cells.

Applicant also asserts about "Long Standing Need and Commercial Success" of the seeds.

The relevance of long-felt need and the failure of others to the issue of obviousness depend on several factors. First, the need must have been a persistent one that was recognized by those of ordinary skill in the art. In re Gershon, 372 F.2d 535, 152 USPQ 602, 605 (CCPA 1967). The alleged problem in this case is migration of seeds from the implantation site, and the prior art also discloses the brachytherapy devices capable of retaining integrity throughout the period of active emission of radiation (i.e., minimizes the chance of migration of implanted seeds within a patient's body). And further, the invention must in fact satisfy the long-standing need. In re Cavanagh, 436 F.2d 491, 168 USPQ (CCPA 1971).

Objective evidence of nonobviousness including commercial success must be commensurate in scope with the claims. In re Tiiffin, 448 F.2d 791, 171 USPQ 294 (CCPA 1971). In order to be commensurate in scope with the claims, the commercial success must be claimed features, and not due to unclaimed features. Joy Technologies Inc. v. Manbeck, 751 F. Supp.225, 229, 17 USPQ2d 1257, 1260 (D.D.C. 1990), aff'd, 959 F.2d 226, 228, 22 USPQ2d 1153, 1156 (Fed. Cir. 1992)

The instant claim 36, a seed for implantation into a subject, wherein the seed is a combination product comprising a biocompatible carrier, one or more therapeutic components, an imaging, radiopaque, or diagnostic marker, and one or more means to maintain location or orientation of the seed upon implantation. The claim does not say anything about anchorseed and the feature recited in the commercial success product is

for anchorseed designed to help reduce seed misalignment and seed migration. The examiner does not know the composition of the anchorseed and also to compare it with the instant claims.

An affidavit or declaration attributing commercial success to a product or process "constructed according to the disclosure and claims of [the] patent application" or other equivalent language does not establish a nexus between the claimed invention and the commercial success because there is no evidence that the product or process which has been sold corresponds to the claimed invention, or that whatever commercial success may have occurred is attributable to the product or process defined by the claims. Ex parte Standish, 10 USPQ2d 1454, 1458 (Bd. Pat. App. & inter. 1988). Furthermore, the success of an embodiment within the claims may not be attributable to improvements or modifications made by others. In re Vamco Machine & Tools, Inc., 752 F.2d 1564, 224 USPQ 617 (Fed. Cir. 1985).

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b). Claims 36-40, 45, 47-55 are rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-3, 5,10,12,13, 30, 32, 35, 38 and 41 of US 6,746,661 B2. Although the conflicting claim is not identical, they are patentably distinct from each other because claim of the instant application is drawn to a brachytherapy seed for implantation into a subject comprising, a biocompatible carrier, one or more therapeutic components, an imaging, radiopaque or other diagnostic marker, and one or more structures to prevent migration, wherein the seed is elastic and has size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10gauge), while the US pat. Application is a branchy therapy seed for implantation into a subject comprising one or more micropsheres, wherein each microsphere comprises at least one component selected from the group consisting of biocompatible component, a therapeutically active component and a radiopaque marker; and brachytherapy seed has a size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10 gauge). Both require brachytherapy seeds, biocompatible component, radiopaque marker and therapeutic agent. Thus, the instant claim is within

the scope of the claim of the US pat. 6,746,661. Thus scope is overlapping each other and properly included in the rejection because hey are patentably distinct from each other. Thus, the claim is readily envisaged by the teaching of the prior art and the claim is properly included in the rejection.

Applicant's arguments filed on 05/16/2008 have been considered but they are not persuasive.

Applicant asserts that brachytherapy seeds formed of biodegradable polymer have elastic properties and other distinct structures for maintaining the location of the seed.

This argument is not found persuasive since the polymers used in the instant claims and polymers disclosed in US 6,746,661 are biodegradable polymers and would have the elastic properties. And further, the US 6,746,661 is silent about the migration of seeds from the implantation site (for maintaining the location of the seed). Thus, the instant claim is within the scope of the claim of the US Pat. 6,746,661. Thus scope is overlapping each other and properly included in the rejection because they are patentably distinct from each other. Thus, the claim is readily envisaged by the teaching of the prior art and the claim is properly included in the rejection. Accordingly, ODP is maintained.

Conclusion

1. No claims are allowed at this time.

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr